REMARKS

Claims 1 to 11 are pending, with claims 8 to 11 withdrawn from consideration as allegedly drawn to a non-elected invention.

Regarding the claim amendments

Claims 2 and 3 have been amended herein to recite an "IgA anti-OmpC antibody" rather than an "antibody to the OmpC antigen." This amendment is supported throughout the specification, for example, at page 7, lines 14-19, which discloses that the presence of IgA anti-OmpC antibodies indicates that the subject has Crohn's disease, and in the concluding phrase of original claim 2.

Claim 3 further has been amended to indicate that the recited OmpC antigen includes the amino acid sequence SEQ ID NO: 1. The amendment to claim 3 is supported throughout the specification, for example, at page 5, lines 22-23, which indicates that *E. coli* OmpC has the amino acid sequence SEQ ID NO: 1.

As set forth above, the amendments are supported in the specification and claims as originally filed and do not add new matter. Applicants therefore respectfully request that the Examiner enter the amendments.

Regarding the § 112, first paragraph, rejection

The rejection of claims 1 to 7 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. The Office Action acknowledges that the specification enables the combined use of IgA OmpC, ASCA, I-2 and pANCA as diagnostic markers for Crohn's disease, yet asserts that the specification fails to enable detection of IgA anti-OmpC antibodies, alone, for diagnosis of Crohn's disease. In particular, the Office Action asserts that the specification only provides that the presence of IgA anti-OmpC antibody is contributory to the diagnosis of Crohn's disease, and further asserts that, throughout the specification, the combination of other markers together with IgA anti-OmpC antibodies is taught for diagnosing Crohn's disease.

Applicants respectfully disagree and submit that the subject application enables the invention as claimed. Firstly, the specification teaches methods for diagnosing Crohn's disease based on detection of IgA anti-OmpC antibodies, without mention of any other diagnostic marker. See, for example, page 3, lines 14-33, and page 7, line 14, to page 8, line 7, which disclose methods of diagnosing Crohn's disease by determining the presence or absence of IgA anti-OmpC antibodies, where the presence of the IgA anti-OmpC antibodies indicates that the subject has Crohn's disease. Secondly, in addition to disclosing a highly sensitive cumulative system based on four markers for detecting 86% of patients with Crohn's disease, the specification also teaches that "IgA OmpC reactivity itself detected 55% of patients having Crohn's disease (page 6, lines

19-21; emphasis added). From the above, it is clear that the specification provides guidance to the skilled person regarding diagnostic methods based on IgA anti-OmpC antibodies, alone, as well as other methods based on the combined use of IgA anti-OmpC antibodies with other diagnostic markers.

The Examiner notes that page 6 of the specification indicates that IgA OmpC antibody reactivity together with ASCA, I-2 and pANCA reactivity provides a "highly sensitive" diagnostic system. Applicants would draw the Examiner's attention to the fact that rejected claims 1 to 7 are not directed a "highly sensitive" diagnostic system. In the subject application, both "highly sensitive" and less sensitive diagnostic methods are disclosed.

Furthermore, as argued previously, Applicants maintain that the claimed methods need not be highly sensitive, nor accurately diagnose all patients having Crohn's disease in order to be enabled. Given that it is fundamental to the rejection, Applicants respectfully request that the Examiner cite a source for her implied assumption that a diagnostic method must be 100% sensitive in order to be patentable. Applicants maintain that anti-OmpC antibodies are present in a large subset of patients with Crohn's disease and can serve to diagnose Crohn's disease where they are present. In this regard, the specification teaches that IgA anti-OmpC antibodies were present in 56% of patients having Crohn's disease but in only 1 of 26 individuals without Crohn's disease (page 7, Table 2, and Figure 4). Furthermore, the ability of anti-OmpC antibodies to serve as a diagnostic marker for Crohn's disease where they are present is

summarized in the concluding phrase of claim 1, "where the presence of said IgA anti-OmpC antibodies indicates that said subject has Crohn's disease." Thus, while the absence of IgA anti-OmpC antibodies may not be meaningful, the presence of IgA anti-OmpC antibodies indicates a diagnosis of Crohn's disease.

Applicants maintain, and respectfully ask that the Examiner address, the assertion that a positive diagnosis of Crohn's disease in any percentage of patients is valuable and that there is no requirement that diagnostic methods be 100% sensitive. The claimed methods do not recite and are not limited to diagnostic procedures which serve to detect 100% of patients with Crohn's disease. It is therefore improper for the Examiner to reject the claims on this basis.

In sum, the specification teaches that detection of IgA anti-OmpC antibodies can be used alone to diagnose more than half (approximately 56%) of individuals with Crohn's disease. These patients need not be analyzed for other antigenic responses in order to come to a determination that the patient has Crohn's disease, potentially sparing the patient from needless additional procedures and expense. Thus, claims 1 to 7 are enabled as written.

In view of the above remarks, it is respectfully requested that the Examiner reconsider and remove the rejection of claims 1 to 7 as allegedly lacking enablement. under 35 U.S.C. § 112, first paragraph.

Regarding the § 112, second paragraph, rejections

The rejection of claims 2 to 7 under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite is respectfully traversed. Claim 2 is allegedly vague and indefinite for failing to recite that the IgA OmpC antibodies bind to the reactive epitope of the OmpC antigen or its reactive fragment. Similarly, claim 3 is allegedly vague and indefinite for failing to recite that the IgA OmpC antibodies bind to the reactive epitope of the OmpC antigen SEQ ID NO: 1 or a reactive fragment thereof.

Applicants submit that the claims are clear and definite as written and, specifically, that it is clear that an "IgA antibody to the OmpC antigen" is an IgA antibody which binds to a reactive epitope of OmpC. Nevertheless, in order to further prosecution, Applicants have amended claims 2 and 3 to recite that the recited complex contains the OmpC antigen, or reactive fragment thereof, and "IgA anti-OmpC antibody." The amendment to claims 2 and 3 does not alter the scope of the claims. In view of the above remarks and amendments, Applicants respectfully request that this ground for rejecting claims 2 and 3 be removed.

Claim 3 further stands rejected under the second paragraph of 35 U.S.C. § 112 as allegedly indefinite for indicating that the recited OmpC antigen has "substantially" the amino acid sequence of SEQ ID NO: 1. While Applicants maintain that claim 3 is clear and definite as written, claim 3 has been amended to delete the term "substantially" in order to further prosecution of the subject application.

Having addressed each ground for rejection, Applicants respectfully request that the Examiner remove the indefiniteness rejection of claims 2 to 7 under the second paragraph of 35 U.S.C. § 112.

Regarding withdrawn claims 8 to 11

In the Office Action dated 10/03/01 (Paper #10), Applicants' election of Group I, claims 1 to 11, and election of the species of SEQ ID NO: 1 are acknowledged. Claims 12 and 13, which have since been canceled, were withdrawn from consideration as allegedly drawn to a non-elected invention. Claims 8 to 11 were also withdrawn from consideration as allegedly drawn to a non-elected species.

Applicants respectfully remind the Examiner that there is a linking claim (claim 1) linking claims 8 to 11 with claims 1 to 7. Thus, should this linking claim be found allowable, any subject matter directed to the non-elected species which was previously withdrawn from consideration must be rejoined and examined for patentability (MPEP 809).

CONCLUSION

Applicants respectfully request that the Examiner consider the amendments and remarks herein above. Should the Examiner have any questions, she is invited to call the undersigned agent or Cathryn Campbell.

Respectfully submitted,

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